IgG-IgM antibodies based infection time detection of COVID-19 using machine learning models

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ABSTRACT

Over the last two years, most scientists have been researching the solution to the pandemic coronavirus disease 2019 (COVID-19). So, the effective inspection and the rapid diagnosis of COVID-19 provide a mitigation ability to the burden on healthcare systems. These research works focus on detecting and knowing the history of infection in terms of time and developed symptoms. In infections detection, artificial intelligence (AI) technologies increase the accuracy and efficiency of the adopted detection methods. These methods will aid the medical staff in classifying patients, essentially when there is a healthcare resources shortage. This paper proposed machine learning-based models for detecting the time of COVID-19 infection in weeks using the laboratory factors of detected antibodies immunoglobulins G and immunoglobulins M (IgG-IgM). This test is common and helpful in diagnosing the suspected patients who held a negative result for the reverse transcription-polymerase chain reaction (RT-PCR) test. The proposed models consider two machine learning models adopting root mean square error (RMSE) and mean absolute error (MAE) factors. The results show acceptable efficiency of performance that ranges from 80% to 100% for pointing the patient in any week of infection, to reduce the likelihood of transmitting the infection from patients who have developed symptoms but with false-negative RT-PCR test.

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1. INTRODUCTION

The novel coronavirus disease 2019 (COVID-19) pandemic caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which was firstly outbreak in China at the end of 2019 and from there it was spread to the rest of the world, continues until now to pose a critical and urgent threat to global health. As of August 19, 2021, globally, there have been 209, 201, and 939 confirmed cases of COVID-19, including 4,390,467 deaths, reported to world health organization (WHO) [1]. The patient's symptoms, some laboratory tests, and chest computerised tomography (CT) scans have the main parameters to indicate the diagnosis of COVID-19. Furthermore, the real-time reverse transcription-polymerase chain reaction (RT-PCR) assays have also a vital role in the diagnostic process by detecting viral ribonucleic acid (RNA) from throat swab or nasal swab specimens [2]. The main pro of this assay is that there is no need for a live virus in the specimens. But for several reasons, including the time of infection, the quality of collected samples, the quality of the testing machine, the need for specialized staff and reliable laboratories, which led provide a limitation in the assay's role for outbreak containment that in turn increased the rate of false-negative results for the confirmed patient [3].

Due to the similarities in the epidemiological features and clinical genetics between the SARS-CoV-2 and the middle east respiratory syndrome (MERS), the antibodies generation process might be the same [4]. That means the detection of immunoglobulins G and immunoglobulins M (IgG and IgM) antibodies could provide information on the time course of virus infection [5]. From the observed serological responses for the IgM and IgG in COVID-19 patients so the guideline of diagnosis and treatment for COVID-19, which are issued by the Chinese National Health Commission, has been recommended to exploit this rapid test to confirm or exclusion of SARS-CoV-2 infection in suspected patients [2].

Throughout time, different diseases have attacked people, and some are risky enough to cause death. The pandemic COVID-19 affects the world in different fields, such as trade, and health. Recently, life in the world is almost stopped, including work, and travelling. Therefore, there are urgent requirements for solving this problem in different ways. One of the most important is diagnosing the infection with COVID-19 for patients that some do not appear any symptoms. Numerous medical tests and the symptoms can lead to the diagnosis of the infected cases, yet these symptoms and test results can be confused. Thus, the digital and information systems are necessary to solve the prediction problem in the early stages for producing suitable medical treatments [6], [7].

With the two sides of hardware and software, digital systems can provide a beneficial service to the medical field in predicting and diagnosing infected people with COVID-19. This is done in two ways: information systems and digital equipment. First, the information system helps the hospital doctors collect the information that eases the understanding of the behavior of this disease. Moreover, this information provides platforms for detecting the COVID-19 and other diseases efficiently based on the feeding medical information and test results [8]. This is to reduce the pressure on doctors and increase diagnosing accuracy using artificial intelligence (AI)-based technologies [9].

AI technologies increase the accuracy in a notable way by copying human behavior to detect a specific type of disease, including COVID-19. Different methods of AI can be used in this field, such as deep learning and machine learning, due to their efficiency in copying the human behavior, in which the diagnosing is accursed [10], [11]. The machine learning technique is based on building more than one model that can be learned using a dataset related to the subject [12], [13]. These models provide the system with classified and arranged results. These results help in getting the soft decision with more accuracy than the classical methods that adopt the hard decision [14]-[17].

A lot of researchers work on finding an efficient digital diagnosing system for detecting the infected cases of COVID-19. Padoan *et al.* [18] presented a comprehensive study on the ability of MAGLUMI 2000 Plus CLIA assay in measuring the antibodies of IgG and IgM for COVID-19 patients. Different tests were performed on this model, and the gotten results showed the efficiency in measuring the IgG and IgM over time intervals for a number of patients. In [19], the B-LiFe mobile laboratory was adopted in testing the body response in terms of antibodies IgG and IgM for different patients over a one-month time period. The sensitivity of the used kit in discovering the occurrence of these antibodies proved its accepted performance and the high accuracy of COVID-19 infections. On the other hand, a complete study on appearing the COVID-19 antibodies over the time in days was introduced in [20]. All ratios and the probabilities of measuring the total antibodies of IgG and IgM were listed, where the blood samples have been taken from day 1 to day 3 of the first infection. This study showed that patients with developed antibodies could fight the COVID virus, while the dead patients suffer from low constant ratios. In [2], the antibodies of COVID-19 were measured and presented in a report that explained the behavior of bodies with IgG and IgM over the time from the first appearance of symptoms. The IgG appeared after the first week of infection and developed for a long time. Moreover, the IgM appeared to reach the top in the first two weeks and started reducing after a while.

On the other hand, in [21], an intelligent IgG-IgM detection system was proposed with high accuracy. This system worked in two steps. The first one was responsible for detecting the increase of the mentioned antibodies, while the second one was responsible for recognizing the diseases type and the level as well. Moreover, Mendels *et al.* [22] proposed a mobile application that used machine learning technology in detecting the COVID-19 patients based on the measured rapid test of IgG and IgM. The developed application increased the detection accuracy and the precise assurance of positive and negative results.

In the same way, an intelligent COVID-19 detection system was proposed in [23] using the swarm intelligent algorithm, evolutionary algorithms, and cost minimization manual selection. This is to increase the validity of the adopted results and increase the testing speed. A literature survey was prepared in [24], [25] for the research work in the field of using AI technologies in diagnosing COVID-19 patients. This study tackled the prospective and concepts that adopted in producing the detection system intelligently. In [26], the intelligent system was adopted in detecting the patients with COVID-19 depending on the levels of antigens serum. This was another way in detecting using blood samples.

Another study on the presented papers was introduced in [27] to focus on the important issues that face the detection of COVID-19 infection cases. Thus, it considered these papers that solved the issues using

intelligent systems that enhance the detection accuracy and time required. In [28], two intelligent models were proposed to detect COVID-19 infections. These models used deep learning and machine learning in diagnosing the infections based on CT-scan images. The proposed system worked in two steps system that used the two models in the detection depending on the types of images. Moreover, Li *et al.* [29] adopted the deep learning model in detecting the infected lung images of infected COVID-19 patients. They considered images were the pulmonary CT scan dataset for high-resolution purposes. Deep literature on the use of intelligent algorithms in detecting infected cases for low living level countries was presented in [30]. The study focused on the type of AI methods and the images used for detecting. In addition, Harmon *et al.* [31] used datasets from different countries to support the training data in modelling and learning the proposed intelligent systems. This could enlarge the angles of detecting the COVID-19 patients.

In this paper, COVID-19 cases are diagnosed in terms of infection time in a week using the proposed machine learning-based detection system based on the IgG and IgM antibodies test results. These results are fed to the machine learning models to fix the right week time of the first COVID-19 infection. The machine learning models are learned using a dataset of real cases in a hospital with IgG and IgM results. The implementation results of the proposed detection system show a satisfying efficiency in diagnosing the time of COVID-19 infection in a week.

2. PROPOSED SYSTEM

In this paper, the detection of the COVID-19 infection time in weeks is considered to be sure that the patient with negative RT-PCR tests can be confirmed. And that’s in turn, decreases the possibility of spreading the infection by people who carry the virus and whose infection has not been confirmed by the RT-PCR tests. This section illustrates the proposed system under four sub-sections as follows.

2.1. The proposed system structures

Figure 1 shows the block diagram of the proposed system. It includes the following:

- The dataset is an important factor in the success of the proposed detection system that adopts machine learning technology. The dataset is divided into two parts: training data of 80% and testing data of 20%.
- These data are entered into the designed algorithm of machine learning that includes algorithm and evaluation as a correction loop.
- The results are fed to the system model that receives the real-time production data from samples of patients needed for the test to produce the week of infection of COVID-19 for patients.

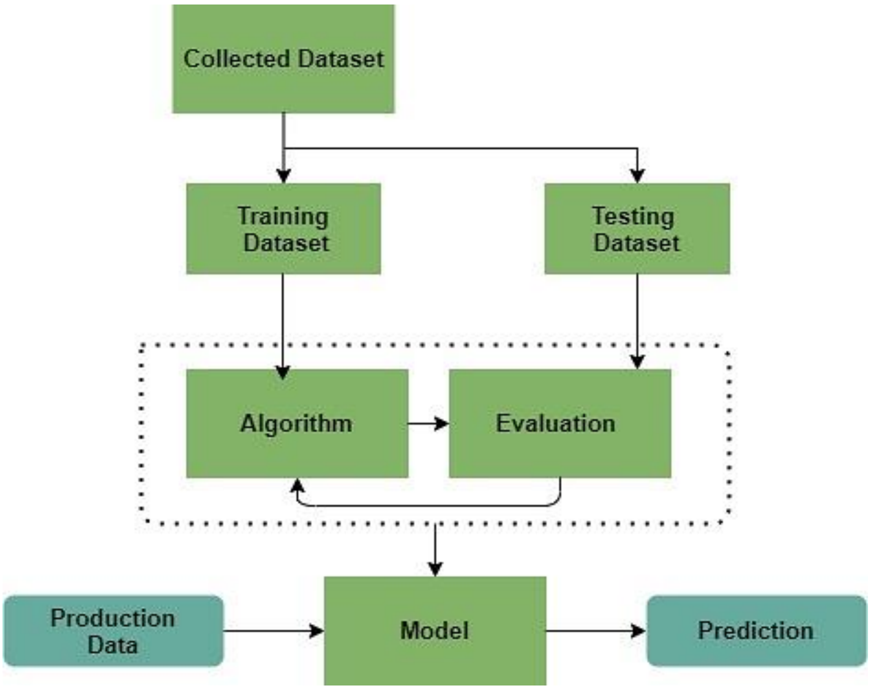

Figure 1. The proposed system structure block diagram

2.2. Dataset

This paper adopts the basis for determining the data gathering process type. Due to the nature of the ideology of the proposed system that adopts the finding of the infection week, a collected dataset from health centres of [32] is considered. This dataset contains 425 samples taken from 285 patient, represented as a comma-separated values (CSV) file to be read and used by the Python library, Panda tool. The Baseline characteristics of the dataset's patients are illustrated in Table 1. The collected dataset needs pre-processing steps for preparing it as an adopted dataset [33]. The most common issues include large values, missing data, noisy data, or unorganized text data.

One of the essential steps in designing a machine learning system is the pre-processing of the gathered data due to its effective role in model accuracy [34]. In simple words, data pre-processing is a process of cleaning and making the raw data more suitable to be used in model training. Due to the multiple types of data that can be included in the dataset, the conversion process is one of the basic pre-process techniques. In this process, and as known that the machine learning model can handle only the numeric type of data, the categorical data of the used dataset in the proposed system are converted to numeric features. As the next process in this step, the missing values of the used dataset are ignored instead of filling them by the manual procedure as common to keep the real state of the collected data. A total of 363 valuable samples are presented to the next stage of researching the best-fitted model for the type of data.

The main goal when designing the machine learning model is to select and find the best model that fits with the used dataset [34]. Between the supervised and unsupervised learning types, the finding of the data type of the used dataset was labelled. Therefore, the perfect usage is founded with the supervised learning model. As well, supervised learning has two categories, which are classification and regression. Due to the continuous nature of the selected target variable, the regression algorithm and decision tree regressor methods [35] are adopted.

Table 1. Baseline characteristics of dataset's patients [32]

Features	All (N=285)	Severe or critical condition (39)	Non-severe or critical condition (246)
Age range- years	(37-56)	(46-77)	(36-55)
Gender	Male: 158 Female: 127	Male: 21 Female: 18	Male: 137 Female: 109
Incubation period-days	(5-12)	(8-10)	(5-12)
Comorbidities			
Hypertension	41	7	34
Cardiovascular disease	9	3	6
Diabetes	22	7	15
Malignancy	3	1	2
Chronic kidney disease	2	0	2
Chronic liver disease	17	5	12
Hyoxemia	4	2	2
Tuberculosis	6	1	5
Signs and symptoms (N of patients)			
Fever	168	24	144
Fatigue	79	20	59
Dry cough	157	22	135
Anorexia	66	18	48
Myalgia	35	5	30
Dypnca	19	14	5
Expectoration	66	14	52
Pharyngalgia	30	2	28
Diarrhea	25	4	21
Nausea	17	4	13
Dizziness	24	6	18
Headache	30	4	26
Vomiting	7	2	5
Abdominal pain	6	2	4
Chill	43	7	36
Nasal congestion	10	2	8
Rhinorrhea	13	2	11
Chest stuffiness	42	8	34
Heart rate range (bpm)	(80-97)	(84-96)	(78-97)

2.3. The proposed algorithm

It is well known that the algorithms can be written in a different style to represent the contains understandably. Figure 2 represents the proposed algorithm that manages the proposed COVID-19 infection week system as a workflow chart.

The adopted work step can be summarized as:

– Collecting the dataset from the considered resources.
– Checking the validity of the collected dataset. It works in a feedback loop with the collecting to make sure that all received data is valid for use in the machine learning models.
– The obtained data is fed to the designed two machine learning models to be applied.
– Checking the results of the two models of machine learning. This step has a feedback link to the stage of applying the machine learning models for ensuring validity.
– These results are entered into the checking model that checks the input of-line samples with the trained output. The input samples contain the IgG and IgM readings of patients after processing the blood samples.

The output results can tell the week of infection of these samples.

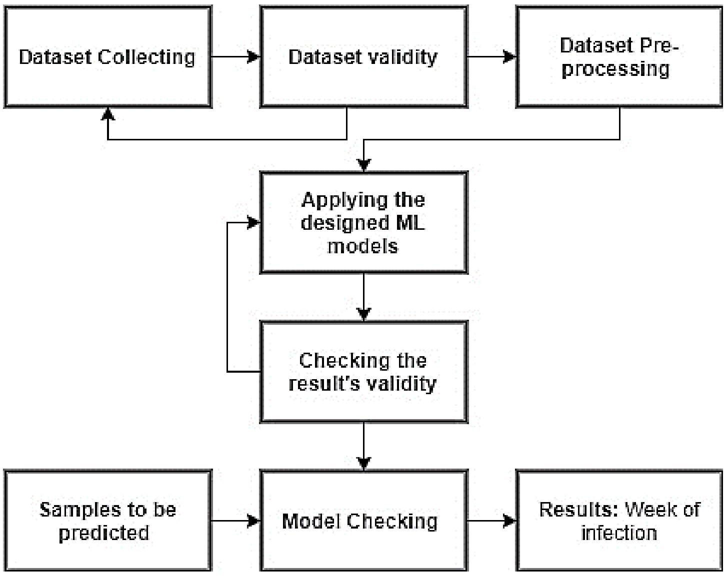

Figure 2. The proposed algorithm workflow

2.4. Machine learning models

As explained in the past sections, the proposed system adopts two machine learning models for computing the week of infection in COVID-19. These models adopt the root mean squared error (RMSE) and mean absolute error (MAE) values between the trained and the tested data. The RMSE can be computed using [36]:

$$RMSE = \sqrt{\frac{\sum_{i=1}^{N}(x_i - \breve{X_i})}{N}} \tag{1}$$

Where N is the total number of samples, x_i is the trained sample, and $\breve{X_i}$ is the tested one. While the MAE is computed as [36]:

$$MSE = \frac{\sum_{i=1}^{N}|(x_i - \breve{X_i})|}{N} \tag{2}$$

The designed models of machine learning are:

– Decision Tree Regressor model (with RMSE = 4.3 and MAE = 3.29).
– Random Forest Regressor model (with RMSE = 4.11 and MAE = 3.21).

These models are well known, and the RMSE and MAE values for each model are obtained by experiment.

3. RESULTS

The proposed detection system's performance is tested under the consideration of ten case studies. These ten cases are represented by the values of IgG and IgM factors for patients (suspected) to have COVID-19 virus. Different software environments are utilized to design the simulator that simulates the real case of the designed models.

The obtained results, that point out the week of infection of the considered patients, are shown in Figure 3. These results are the average values of the RMSE and MAE for each case often. From the Figure 3, it is shown that the infection week of ten cases with one day after symptoms appear. The days with the cases represent the real days of infection, while the patterned bars are the weeks from 1 to 4. The designed models of machine learning decide the week of infection that is shown in the four-week pattern. It is concluded that most cases are detected with exact the week of infection, except cases 3 and 7. These cases happened on days 8 and 6, respectively; thus, they are close to the next and last week.

For more testing and evaluating the proposed system, Table 2 illustrates the efficiency of a different number of cases that are tested using the designed machine learning models. This table shows various efficiency ratios, and this has happened for different reasons, including:

- The day that sample is taken after symptoms appear.
- The real day of infection can be the trade of cases between two weeks.
- The sample data is not valid.

Therefore, the results are varied between 80% to 100%. The efficiency is computed as:

$$Efficiency = \frac{No.of\ right\ decision}{Total\ samples} \tag{3}$$

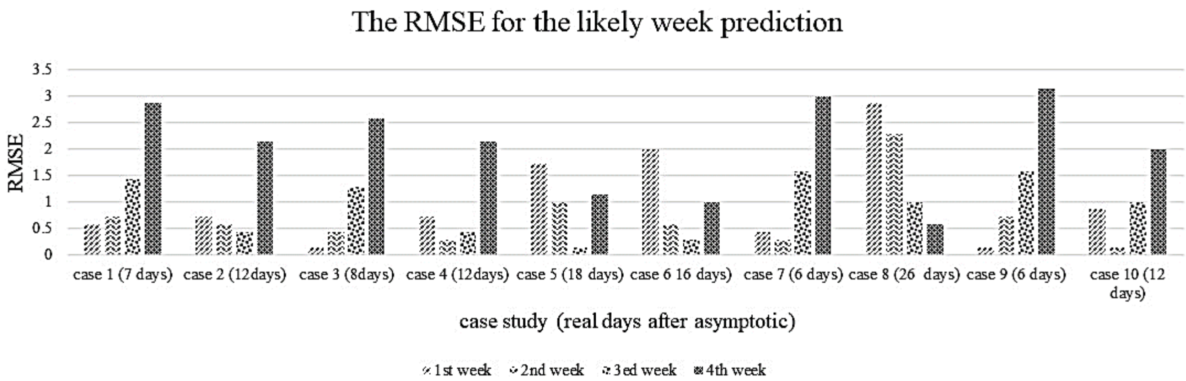

Figure 3. Average of RMSE values for ten cases and the week decision

Table 2. The designed machine learning models' efficiency of a different number of cases

No. of sample	Sampling time	No. of right decision of infection week	Efficiency
10	1-2 days	8	80%
30	1 day	29	97%
50	2 days	47	94%
100	1 day	99	99%
150	1 day	140	94%
200	1 day	193	97%
210	1 day	204	97%
220	1 day	220	100%
300	1 day	298	99%
400	1 day	396	99%

4. CONCLUSION

An infection week of the COVID-19 detection system was proposed based on machine learning models. The used training dataset was pre-processed to introduce valid data ready for the designed models. The designed machine learning models adopted the decision tree regressor and random forest regressor models with the MSER and MAE values (4.3, 4.11) and 3.29, respectively, as a tradeoff threshold for decision. The proposed system proved its ability in detecting the right week of infection, as shown in the considered results. The obtained results illustrated the proposed system's efficiency in the range of 80% to 100% depending on the day of sampling and the infection day that can be between two weeks.

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